an atomic structural model of a TR LBD isoform bound to a test compound, wherein said atomic structural model is generated utilizing data from Appendix 3, 4, 5, 6, 7 or 8,

screening said test compounds in a biological assay for TR isoform activity characterized by binding of a test compound to a TR LBD isoform, and

identifying a test compound that selectively modulates the activity of a TR isoform, with the proviso that said [molecule] compound, is other than a thyronine or thyronine-like compound disclosed in a reference cited in Appendix I.

a4 cont

41. (Amended) A peptide, peptidomatic or synthetic [molecule] compound that selectively modulates the activity of a thyroid hormone receptor (TR) compared to other nuclear hormone receptors, identified by the method [of any one of claims 19 or 40,] comprising:

modeling compounds which fit spatially into a TR ligand binding domain (TR LBD) using an atomic structural model of a TR LBD, wherein said atomic structural model is generated utilizing data from Appendix 3, 4, 5, 6, 7 or 8,

selecting a compound comprising conformationally constrained structural features that interact with conformationally constrained residues of a TR LBD,

identifying in a biological assay for TR activity a compound that selectively binds to a TR LBD compared to other nuclear receptors, whereby a compound that selectively modulates a TR is identified, with the proviso that said [molecule] compound is other than a thyronine or thyronine-like compound disclosed in a reference cited in Appendix I.

a5

Please insert the following claims:

a6

--61. A peptide, peptidomimetic or synthetic compound wherein said compound is a thyroid hormone receptor (TR) agonist or antagonist ligand, identified by the method comprising the steps of:

providing the atomic coordinates of a TR ligand binding domain (TR LBD) to a computerized modeling system, wherein said atomic coordinates are generated utilizing data from Appendix 3, 4, 5, 6, 7 or 8;

modeling ligands which fit spatially into the TR LBD; and

identifying in a biological assay for TR activity a ligand which increases or decreases the activity of said TR, whereby a TR agonist or antagonist is identified,

with the proviso that said compound is other than a thyronine or thyronine-like compound disclosed in a reference cited in Appendix I.

62. A peptide, peptidomatic or synthetic compound wherein said compound is a thyroid hormone receptor (TR) agonist or antagonist ligand that selectively modulates the activity of a TR compared to other nuclear receptors, identified by the method comprising the steps of:

providing the atomic coordinates of a TR ligand binding domain (TR LBD) to a computerized modeling system, wherein said atomic coordinates are generated utilizing data from Appendix 3, 4, 5, 6, 7 or 8;

modeling ligands which fit spatially into the TR LBD and which interact with conformationally constrained residues of a TR LBD conserved among TR isoforms; and

identifying in a biological assay for TR activity a ligand which selectively binds to said TR and increases or decreases the activity of said TR, whereby a TR agonist or antagonist that selectively modulates the activity of a TR is identified, with the proviso that said molecule is other than a thyronine or thyronine-like compound disclosed in a reference cited in Appendix I.--

a6 Cont.

REMARKS

Page 1 of the Specification is amended to eliminate the duplicative "Cross-reference to Related Applications" and to correctly place the "Acknowledgements" section following the "Cross-reference to Related Applications." Further, the language of the "Cross-reference to Related Applications" has been modified to comport with the requirements of MPEP § 210.11 (version 7, July 1998, pg. 200-55).